REMTEC & EMERGING CONTAMINANTS SUMMIT

OCTOBER 3-5, 2023

An Evaluation of PFAS Avian Tissue Distribution: State of the Science

John Newsted

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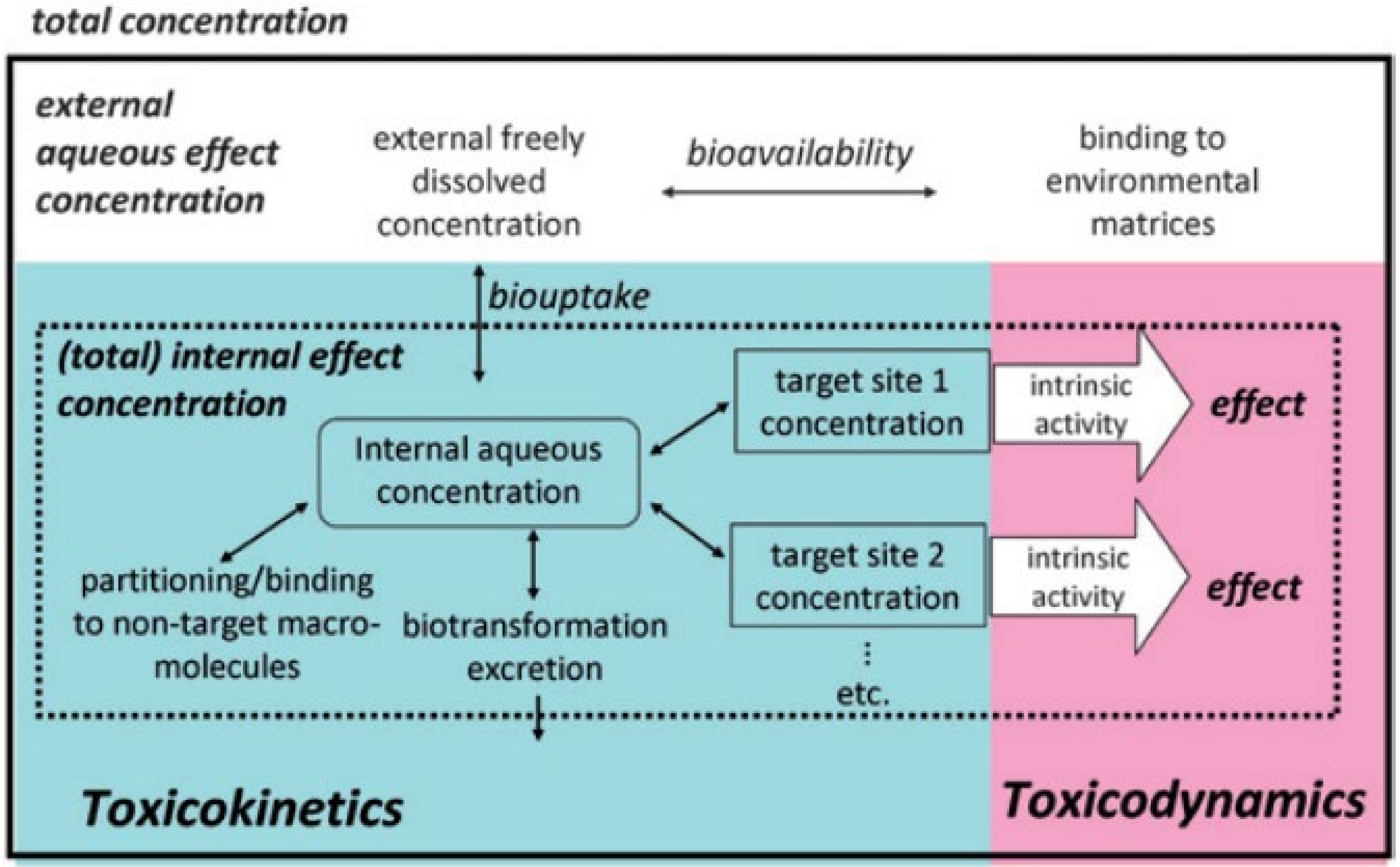
Why Birds?

- Birds have used a bioindicators to evaluate spatial and temporal aspects of environmental contamination
  - Attributes as bioindicators include:
  - They are abundant
  - Wide ranging (local to global distributions)
  - Many are long lived
  - Many species are apex predators
- Are important components of ecological risk assessments in aquatic and terrestrial ecosystems
  - Tissue data are useful in understating spatial and temporal changes in contaminant data
  - Tissue data can also be used to assess the ehalt ha bird population

Tissue Residue Approach (TRA)

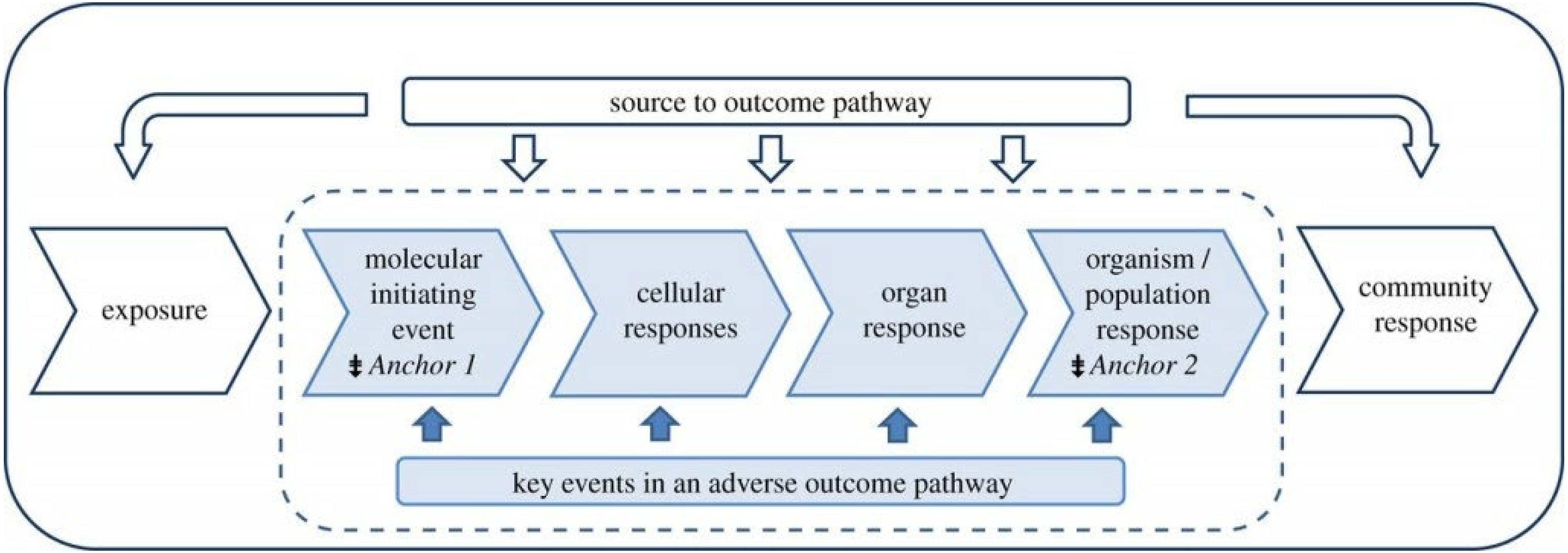
- General concept that groups all aspects in toxicology that consider tissue or internal concentrations as the dose and its relationship to environmental protection
  - Tissue residue metrics are likely to be less variable among species as compared to ambient exposure concentrations
  - Tissue concentrations consider toxicokinetics and bioavailability reducing variability due to differences in environmental conditions
  - Exposure-based toxicity metrics can under the appropriate circumstances can paired with bioaccumulation factors to derive tissue levels
- Tissue Residue values are not replacements for conventional exposure or dose-based method in risk assessments, they are complementary

Process that are involved in the determination of target site concentrations



Echer and Hermens 2002

Adverse Outcome pathways



PFOS Measured in Avian Tissues: Field Studies

Study	Species	Blood	Spleen	Brain	Fat	Heart	Kidney	Liver	Lung	Muscle
Olivero-Verbel et al. 2005	Brown Pelican		X	X		X	X	X	X	X
Robuck et al. 2022	Brown Pelican	X		X	X	X	X	X	X	V
Holstrom et al. 2005	C. Guillemont						X	X		X
Rubarth J et al. 2011	Red-Throated Diver	X	X	X	X	X	X	X	X	X
Chu S et al. 2015	Black-Footed Albatross					X		X		X
Gebbnik WA et al. 2012	Herring Gull	X		X	X			X		X
Robuck et al. 2022	Herring Gull	X		X	X	X	X	X	X	X
Robuck et al. 2022	Royal Gull	X		X		X	X	X	X	X
Robuck et al. 2022	Sandwich Gull	X		X		X	X	X	X	X
Robuck et al. 2022	Great Shearwater	X		X		X	X	X	X	X

PFOS Measured in Avian Tissues: Laboratory Studies

Study	Species	Blood[1]	Spleen	Brain	Fat[2]	Heart	Kidney	Liver	Lung	Muscle
Yeung et al. 2009	Chicken	X					X	X		
Yoo et al. 2009	Chicken	X		X			X	X		X
Kowalczyk et al. 2020	Chicken	X					X	X		
Newsted et al. 2007	Mallard	X						X		
	Bobwhite Quail	X						X		
Bursian et al. 2021	Japanese Quail	X						X		
Dennis et al.	Bobwhite Quail							X		

[1] Blood includes whole, plasma and serum
[2] Fat includes adipose

Factors Influencing Bioaccumulation and Tissue Distribution In Birds

Factors Influencing Protein Binding

Abiotic
- Season
    - Habitat
- Temperature

Biotic
- Diet
- Nutrition
- Disease
- Reproductive Status
- Migratory behavior

Species Differences

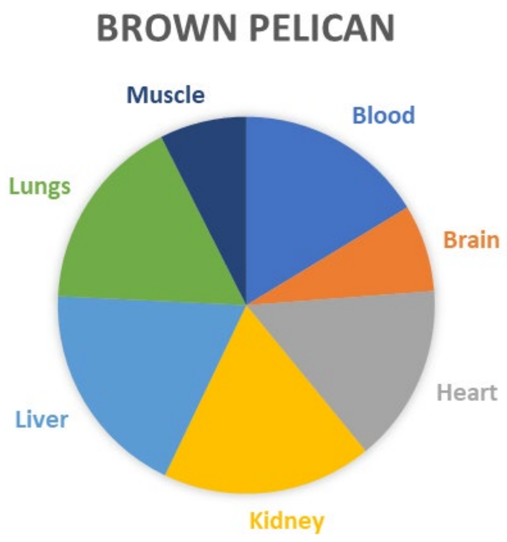
- Tissue protein composition
- Metabolism
- Physiological
    - Renal Function
        - Anion transport
        - Water Regulation
- Hepatic Function
    - Metabolism

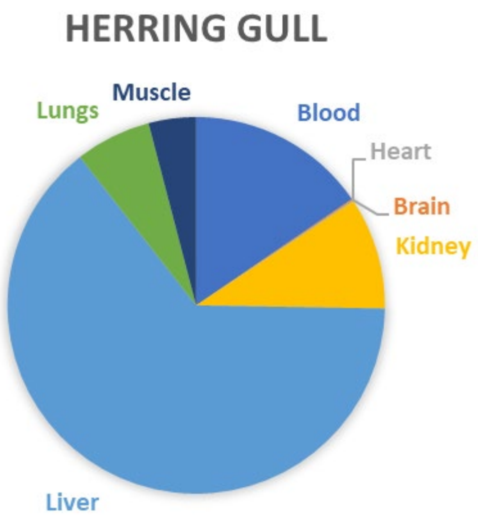
Changes in Physiology

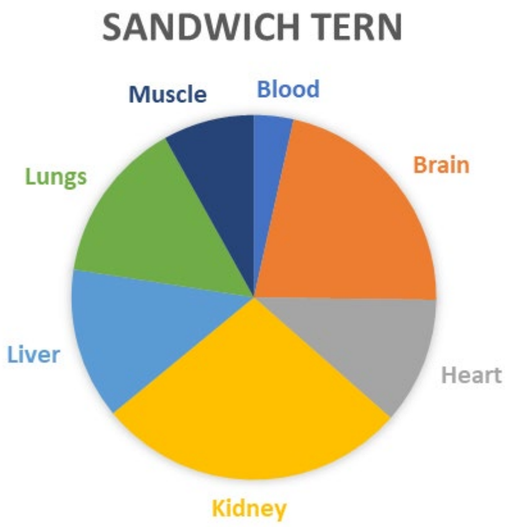
- Protein Expression
    - Fatty Acid Binding Proteins
- Cellular Membranes
    - Phospholipids
    - Phospholipid proteins
- Serum Composition
    - Albumin
    - Protein Transporters
    - Phospholipid proteins
- Transporter Systems
    - Organic Anion Transporters
    - ATP-Cassette Transporters

Adapted from: Bangma JT et al. 2022:Environ. Intern. 159:107037

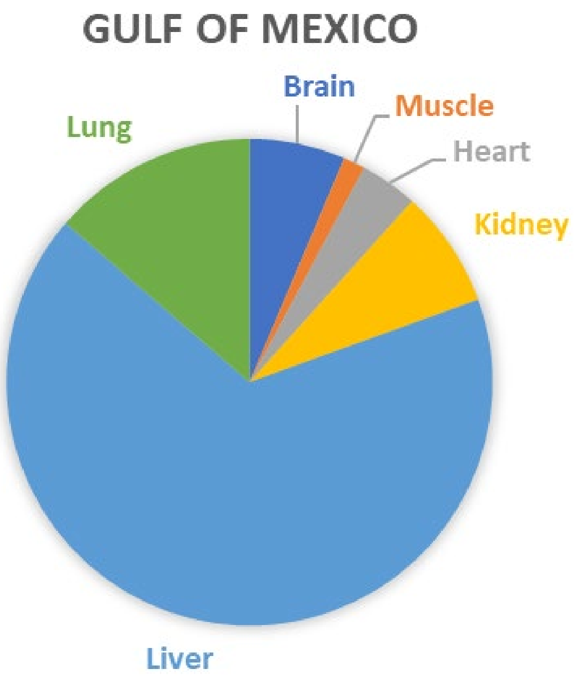
Species Differences in PFOS Tissue Distribution

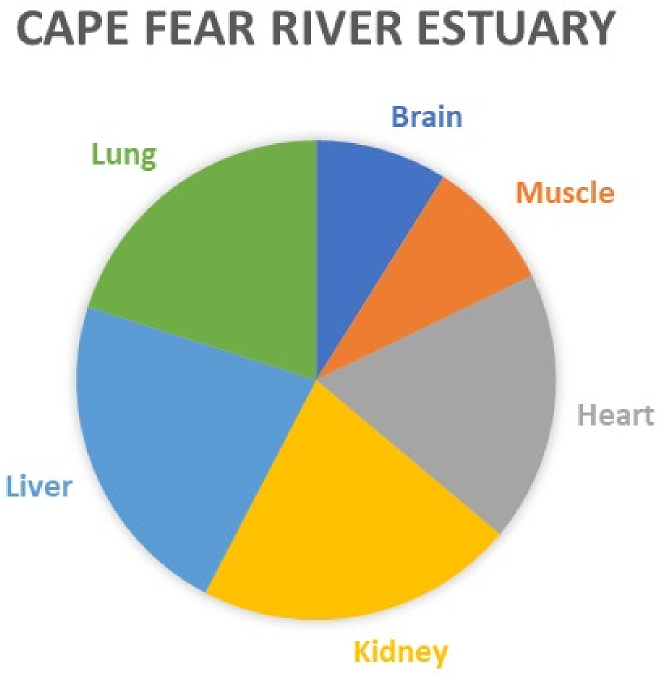






Tissue distribution of PFOS in Brown Pelican





Tissue Liver	GOM	CFRE
Kidney	0.966	0.120
Heart	0.820	0.057
Lung	0.899	0.204
Muscle	0.400	0.020
Brain	0.400	0.100

PFOS Tissue Distribution in Avian Species

Species	Exposure	Liver: Serum Ratio
Northern Bobwhite	Chronic-Definitive	0.596
Mallard	Chronic-Definitive	0.675
Northern Bobwhite	Chronic-Preliminary	0.017
Mallard	Chronic-Preliminary	0.11
Chicken	Pharmacokinetic	1.35
Japanese Quail	Chronic	1.90
Herring Gull	Environmental	3.16
Herring Gull	Environmental	4.15
Red-Throated Diver	Environmental	2.50
Laughing Gull	Environmental	7.54
Brown Pelican	Environmental	1.14
Great Shearwater	Environmental	0.83

Distribution of PFOS in Bird Eggs[1]

Species	Treatment[2] (mg/kg, feed)	Membrane (ng/ml)	Albumin (ng/ml)	Yolk (ng/ml)
Mallard	17.6	342	20	50,700
Quail	17.6	311	14	56,500

[1] Pilot range-finding study for chronic reproduction tests

[2] Birds photostimulated then put on treated diet. Samples collected at week 6.

Partitioning of PFOS in Egg Yolk

Treatment[1]	Fraction	Quail[2]	Mallard
10 mg/kg, feed	Yolk-Whole	62	53
	Yolk-VLDL	40	42
	Yolk-Phosvitin	0.83	8.8
	Yolk-Lipovitellin	1.32	3.6

[1] Chronic dietary study with mallards and quail (Newsted et al. 2007)
[2] Concentration in units of µg/g, wet weight

Are nonlethal sampling approaches suitable for monitoring perfluoroalkyl acids?

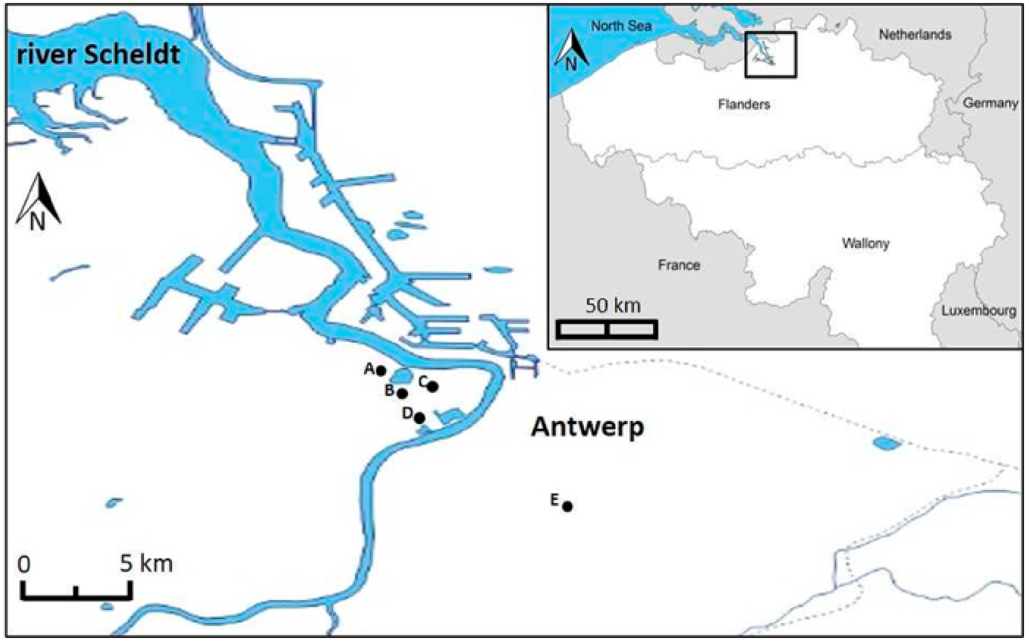
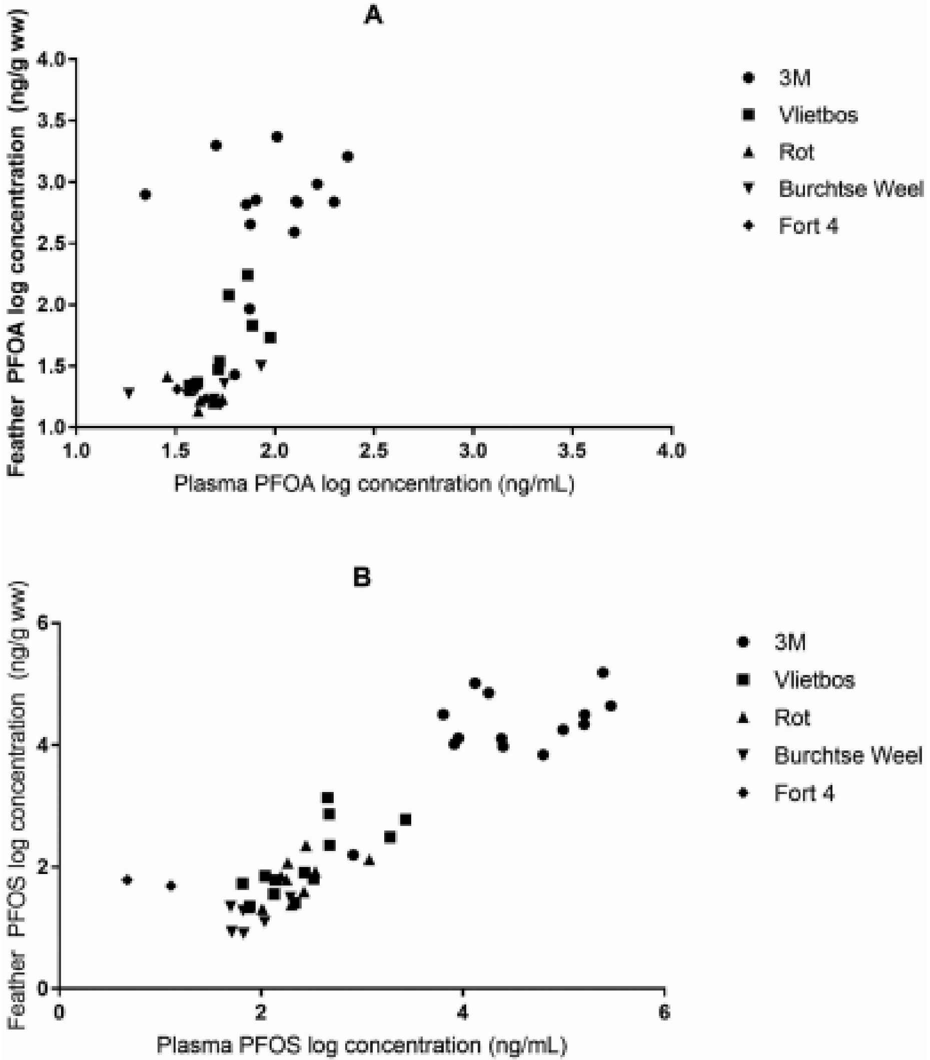


Figure 1. Overview of the study area in Antwerp, Belgium. Sampling locations are indicated as letters: (A) 3M fluorochemical plant, (B) Vlietbos, (C) Middenvijver-Rot, (D) Burchtse Weel, and (E) Fort 4.

Groffen T et al. 2020,EST 54:9334-44

PFAS in Parus major



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Environmental Science & Technology LETTERS

Letter

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Phospholipid Levels Predict the Tissue Distribution of Poly- and Perfluoroalkyl Substances in a Marine Mammal

Clifton Dassuncao,[*,†,‡] Heidi Pickard,[†] Marisa Pfohl,[§] Andrea K. Tokranov,[†] Miling Li,[†] Bjarni Mikkelsen,[||] Angela Slitt,[§] and Elsie M. Sunderland[†,‡]

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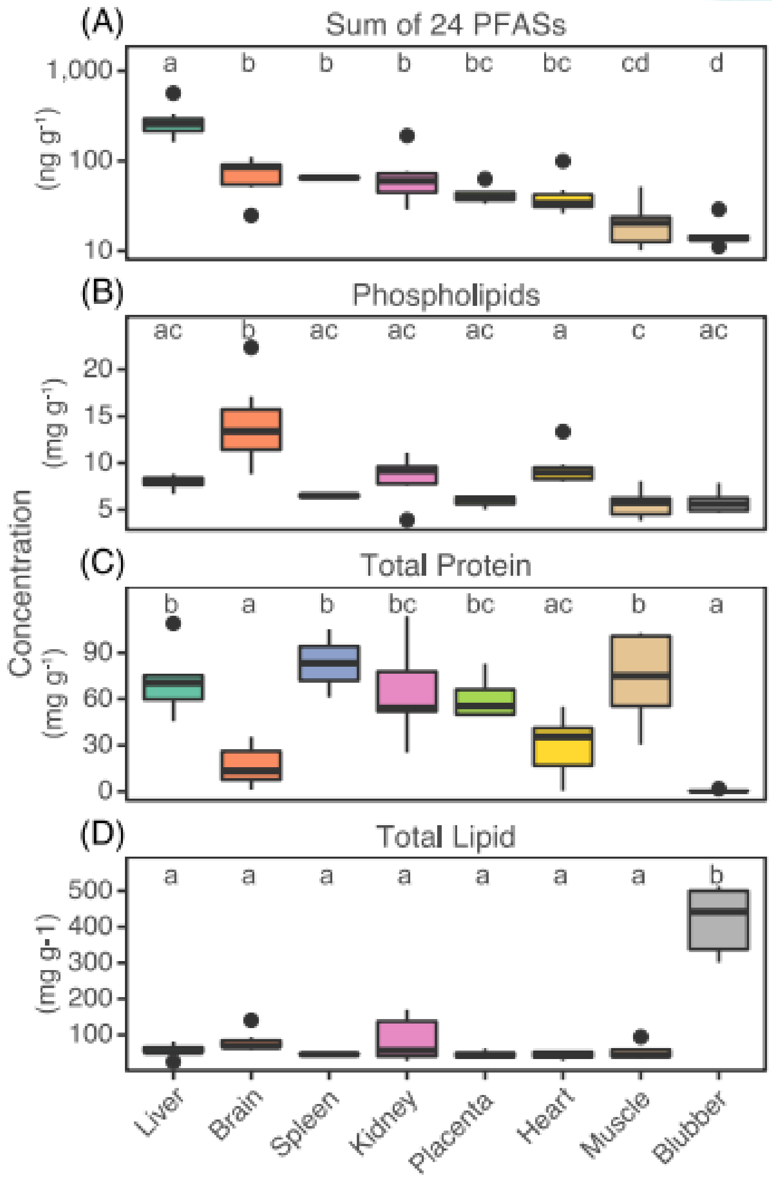
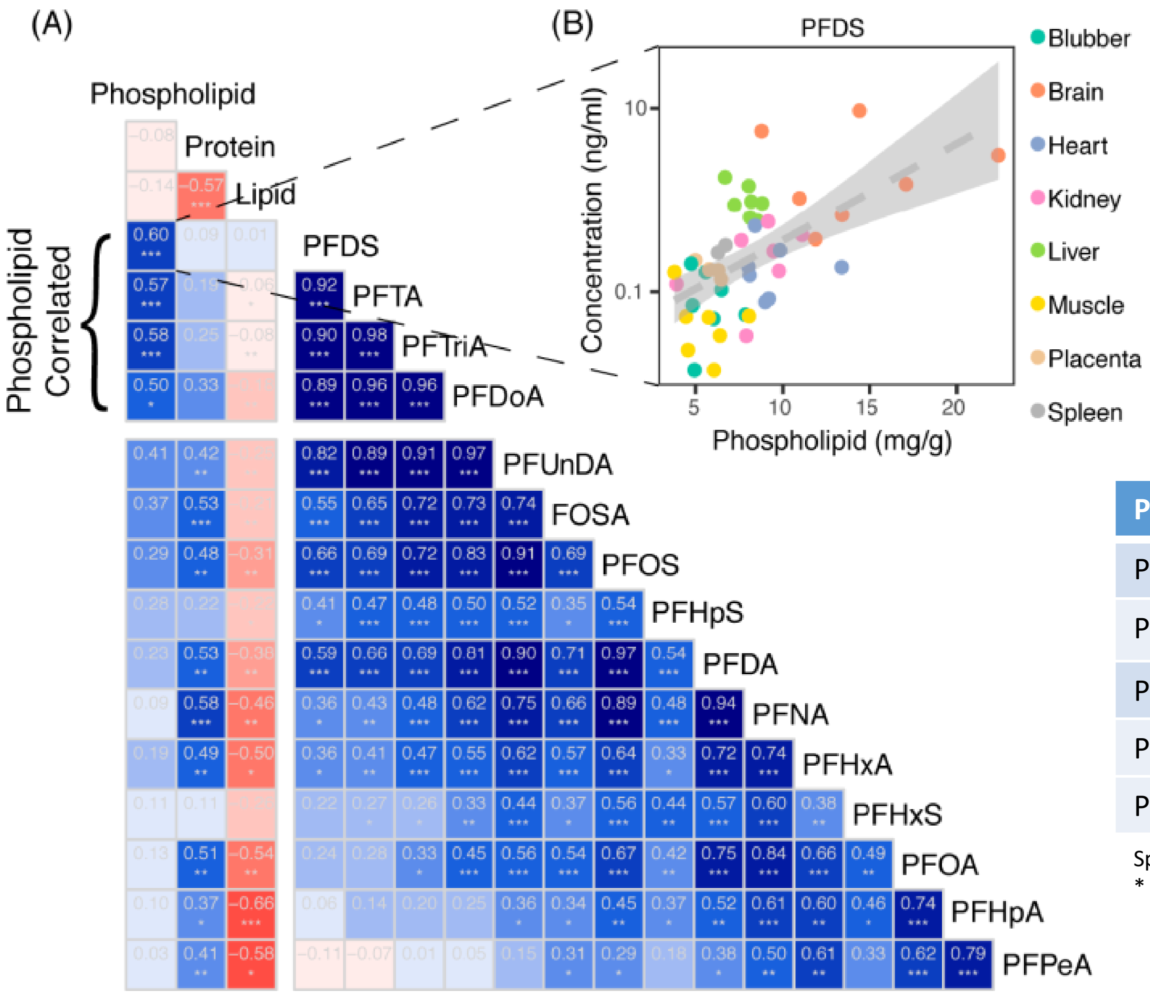


Figure 1. Measured concentrations of (A) the sum of 24 PFASs, (B) phospholipids, (C) total protein, and (D) total lipid in each pilot whale tissue. The dark line within the box represents the median, and box hinges represent the first and third quartiles. The whiskers represent 1.5 times the interquartile range, and black points are outliers. Common letters above each box indicate tissues with no significant difference between group comparisons using Tukey's test.

Spearman correlations between PFAS and phospholipids, protein and lipids in North Atlantic Pilot Whales



PFAS	PL	Protein	Lipid
PFDS	0.60*	0.09	0.01
PFOS	0.29	0.48*	-0.31*
PFOA	0.15	0.51*	-0.54
PFHxS	0.11	0.11	-0.26*
PFHxA	0.19	0.49*	-0.50*

Spearman correlations.
* indicates a significant correlation (P<0.05)

Dassuncao C. et al. 2019: EST Lett 6:119

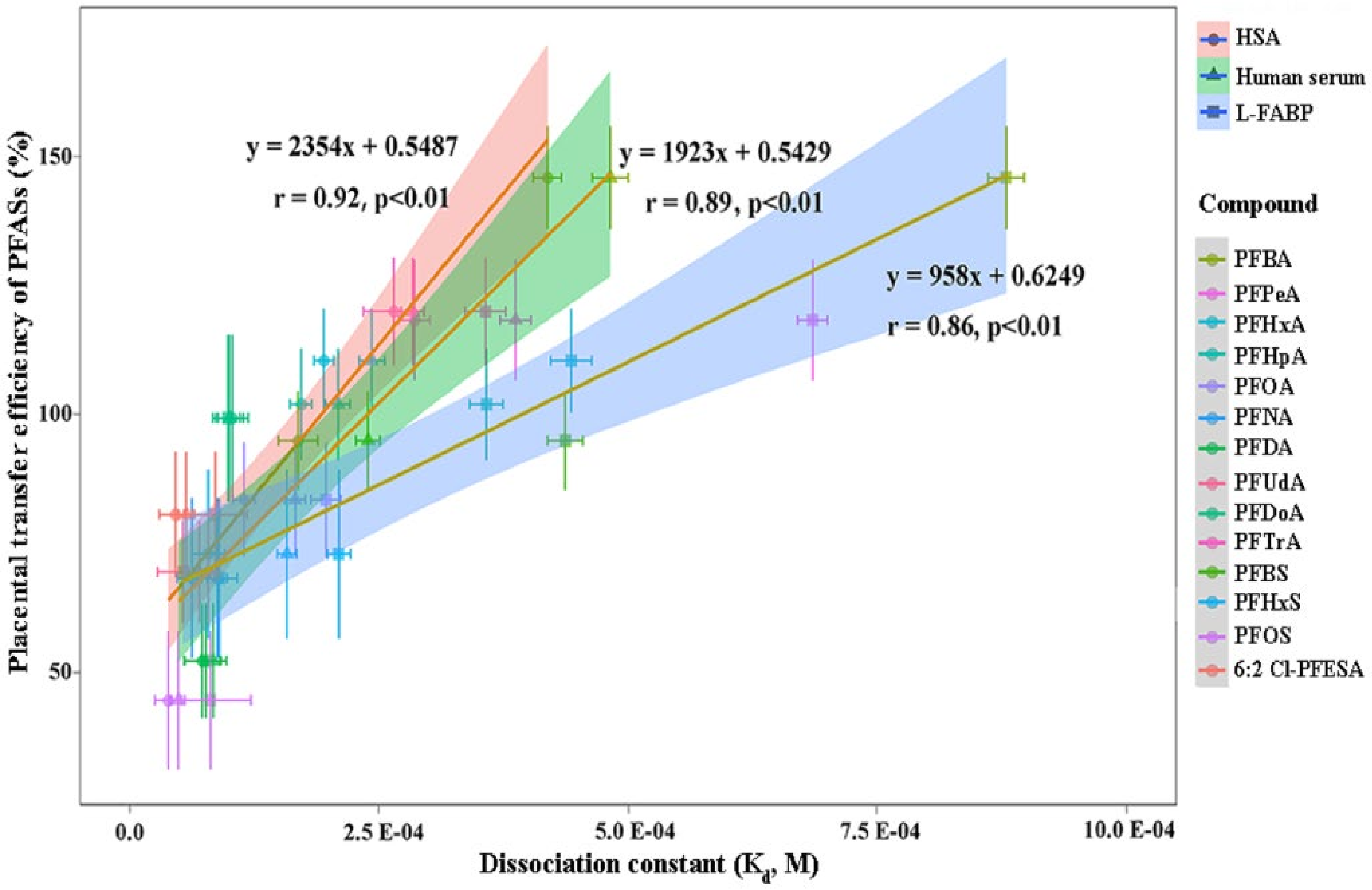
Mixed-Effects regression models for PFAS and phospholipids, proteins, and lipid concentrations[1]

	Model with all tissues			Model without Brain		
PFAS	PL(%)	Protein (%)	Lipid (%)	PL(%)	Protein (%)	Lipid (%)
PFDS	26	-	-	20	-	-
PFTA	22	0.9	-	19	1.2	-
PFTrA	23	1.3	-	23	1.6	-
PFDoA	17	1.3	-	22	1.5	-
PFUnDA	12	1.8	-	24	1.8	-
PFOS	-	1.4	-	25	1.4	-
FOSA	8.5	1.3	-	19	1.3	-
PFNA	-	2.0	-	23	1.6	-
PFOA	-	1.0	-	12	0.6	-
PFHxS	-	-	-	19	-	-

1 Percent changes in PFAS concentration for each mg per gram in PL, protein, or lipid concentration
(-) indicates that relationships were not significant at $p < 0.05$

Dassuncao C. et al. 2019: EST Lett 6:119

Relationship between placental transfer efficiency and human serum protein



PFAS	Kd-HP[1]	Kd-SP	Kd-LP
PFBA	419	482	879
PFPeA	286	387	685
PFHxA	195	243	443
PFHpA	172	209	358
PFOA	115	166	197
PFNA	73	84	90
PFDA	65	70	77
PFUdA	79	75	54
PFDoA	103	100	95
PFTrA	265	284	317
PFBS	169	239	436
PFHxS	79	158	210
PFOS	38	49	81

1 Kds are: HP is HAS-PFAS
SP is serum protein-PFAS
LP is L-FABP-PFAS.

Gao K et al. 2019; EST 53-6529

Chemical Activity

Chemical activity (*a*)Is a unitless thermodynamic quantity that can be used to describe nonideal solutions of chemicals in different phase and media

Can be defined as:

- A ratio of chemical fugacity (*f*: Pa) in environmental media and a reference fugacity (f^R) of a pure chemical at a defined standard state, or
- On a Raoult's law basis, it is the product of the concentration of a chemical (mole of solute/moles of solvent) and activity coefficient γ (unitless)

$$a = f/f^R = \gamma \times X$$

Chemical activity

In neutral organic chemicals γ can be determined from the solubility of that chemicals in water

For substances that are liquid at systems temperatures, γ is the reciprocal of a chemical solubility in a solvent

$$\gamma = 1/X \text{ (solubility in a solvent; moles/moles)}$$

For substances that are solid at system temperatures, γ for a neutral organic is determined as the product of a chemicals solubility and its fugacity ratio(F)

$$\gamma = F \times X$$

Where : $\ln F = -(\Delta H/R)(1/T-1Tm)$

Working concepts for partition into tissues

For PFAS, partitioning is predominately related to their association with:

- Phospholipids in cell membranes (e.g. polar lipids)
- Nonstructural proteins (e.g.. Albumin, LFBPs ,etc),
- Structural proteins (e.g. collagen, myosin, and actin)
- Water
- Neutral lipids (storage fats)
    - Minor component for most PFAS classes

To determine the accumulation of PFAS into an organism or organ, the sorptive capacity can be determined as follows:

$$S_{organism} = \psi_{nl} \times S_{nl} + \psi_{pl} \times S_{pl} + \psi_{alb} \times S_{alb} + \psi_{sp} \times S_{sp} + \psi_{w} \times S_{w}$$

Where:

- ψ represents the percent faction of the tissue of interest
- S is the solubility of a chemical in the tissue of interest
    - Can be approximated using distribution coefficients (log D_{xw}) between tissue and water

Apparent Chemical Activity

$$a_{organism} = \frac{Concentration_{organism}}{Solubility_{organism}} \; x \; F$$

Derivation Conditions

- Chemical activities were derived with no reference phase
- Derivation of organism sorptive capacities used distribution coefficients between water and tissue (Allendorf et al. 2021)
- For PFAS without distribution coefficients, coefficients were predicted using regression models and data from Allendorf et al. 2021
  - Separate regression were used for PFSA and PFCA
- Water solubilities were either measured or predicted (OPERA)

Environmental Science & Technology

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Article

Developing Methods for Assessing Trophic Magnification of Perfluoroalkyl Substances within an Urban Terrestrial Avian Food Web

Katharine M. Fremlin,* John E. Elliott, Robert J. Letcher, Tom Harner, and Frank A.P.C. Gobas

Cite This: *Environ. Sci. Technol.* 2023, 57, 12806−12818

34

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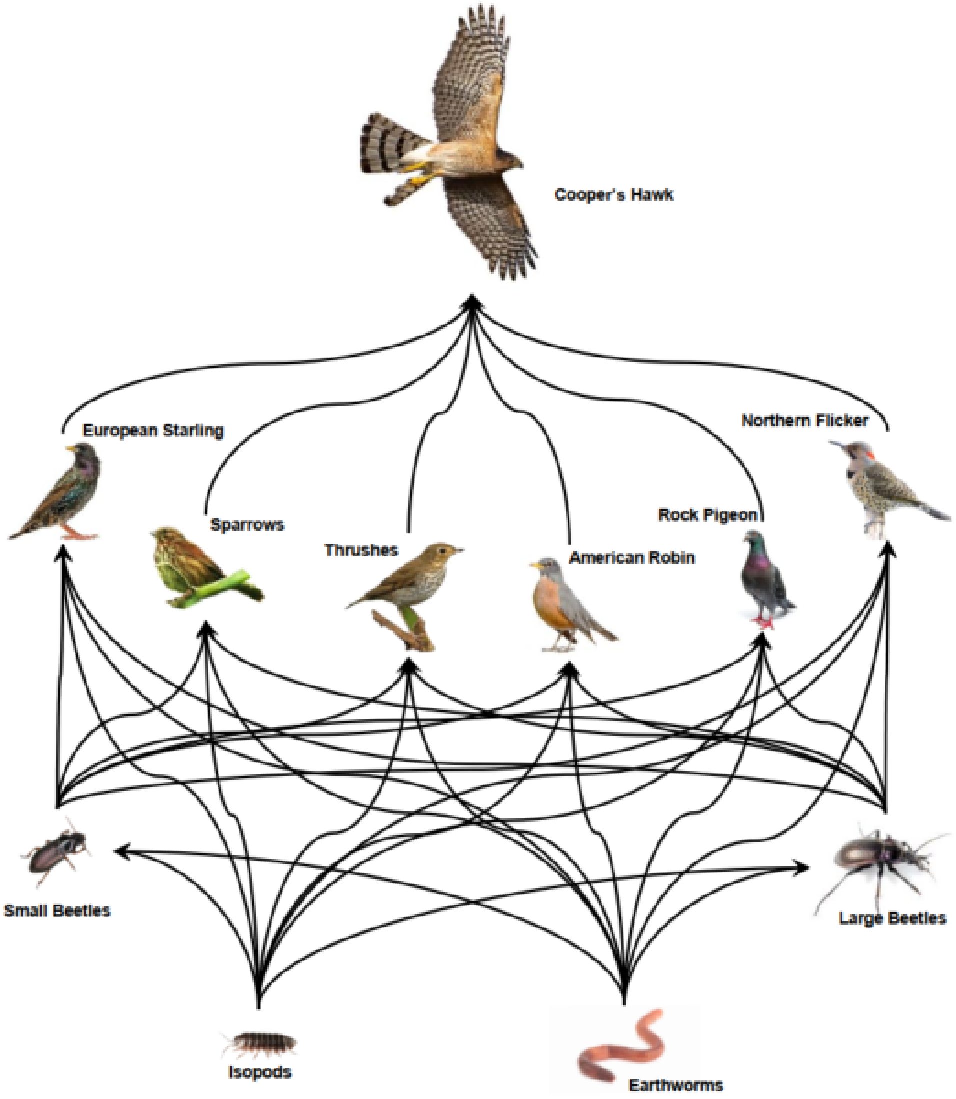


Figure S3. Urban terrestrial avian food-web with generalised trophic linkages among organisms collected in Metro Vancouver, BC in 2016.

Table S1. Species selected from the urban terrestrial food web in Fremlin, et al. [11] with the number of eggs (hawk) or composite samples analysed for PFAS in 2020.

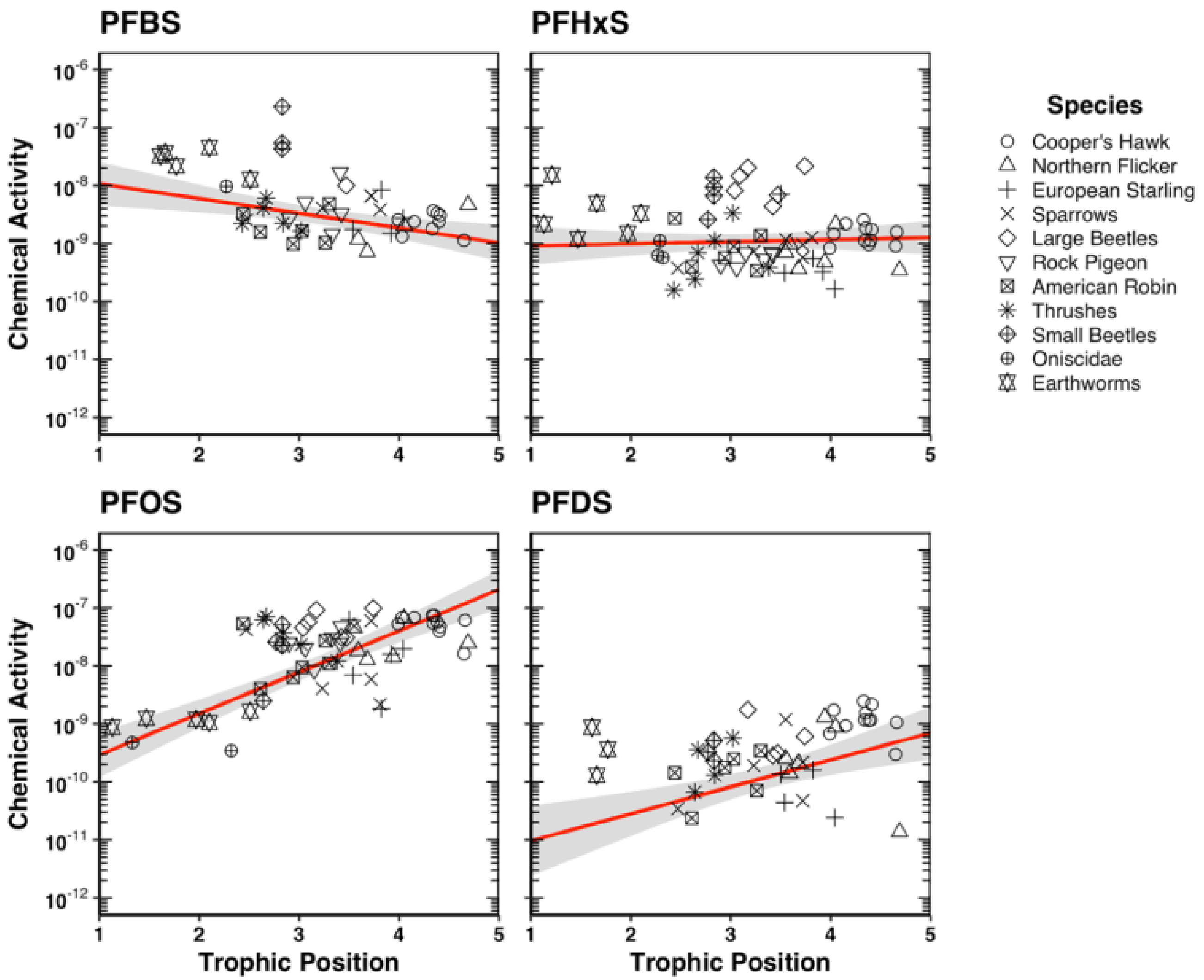
Trophic Guild	Species	Scientific name	*n*
Apex Predator	Cooper's Hawk	*Accipiter cooperii*	12
Secondary Consumers	American Robin	*Turdus migratorius*	6
	European Starling	*Sturnus vulgaris*	5
	Northern Flicker	*Colaptes auratus*	6
	Rock Pigeon, Eurasian Collared Dove	*Columba livia, Streptopelia decaocto*	6
	Sparrows: House Sparrow, Dark-eyed Junco, White-crowned Sparrow, Fox Sparrow, Song Sparrow, Golden-crowned Sparrow, Spotted Towhee	*Passer domesticus, Junco hyemalis, Zonotrichia leucophrys, Passerella iliaca, Melospiza melodia, Zonotrichia atricapilla, Pipilo maculatus*	6
	Thrushes: Varied Thrush, Swainson's Thrush, Hermit Thrush	*Ixoreus naevius, Catharus ustulatus, Catharus guttatus*	6
Primary Consumers	Large Beetles	*Pterostichus melanrius, Carabus nemoralis, Carabus granulatus, Pterostichus sp.*	6
	Small Beetles	*Harpalus affinis, Calathus fuscipes, Anisodactylus binotatus, Agonum mülleri, Philonthus politus, Anatrichis minuta, Amara sp., Staphynlidae, Harpalitae*	5
Detritivores	Earthworms	*Lumbricidae*	12
	Oniscidea: Sowbugs and Pillbugs	*Oniscus asellus, Porcellio scaber, Armadillidium vulgare*	5

Table S14. Linear relationships between trophic position and the mass fraction (%) of each respective tissue in the biota samples. Values in bold indicate statistical significance of *p*-value with α < 0.05.

Tissue	N	Slope	SE	Int	*p*-value	Adj R^2	*Pearson's *r*	AIC	BIC	F Statistic	df
Albumin	74	0.960	0.165	-0.350	**< 0.001**	0.310	0.57	251	258	33.9	1, 72
Neutral Lipid	74	0.925	0.244	0.0277	**< 0.001**	0.155	0.41	309	316	14.4	1, 72
Polar Lipid	74	0.410	0.0630	-0.438	**< 0.001**	0.362	0.61	109	115	42.3	1, 72
Structural Protein	74	0.119	0.0892	1.73	0.186	0.0106	0.16	160	167	1.78	1, 72
Total Lipid	74	1.33	0.241	-0.410	**< 0.001**	0.290	0.55	307	314	30.8	1, 72
Total Protein	74	1.08	0.244	1.38	**< 0.001**	0.202	0.46	309	316	19.5	1, 72
Water	74	-0.523	1.18	74.8	0.660	-0.0111	-0.05	543	550	0.195	1, 72

*Pearson's product moment correlation coefficient

Apparent Chemical Activities
In terrestrial biota



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Final Thoughts

- Laboratory studies are still needed to characterize the underlying factors involved bioaccumulation and tissue distribution of PFAS into birds
  - Evaluation of what proteins, lipids or other cellular constituents are involved in the transport and accumulation PFAS into different tissues
  - These should include intraspecific and interspecific evaluations
  - Normalization approaches for PFAS should consider the scale (population, organism or sub-organism) to better quantify differences accumulation in birds
- Field studies are also needed to better understand the relationships between trophic position and accumulation of PFAS, both on a whole body and tissue specific basis
  - Considerations relative to the ecological aspects of avian species should also be noted and evaluated (reproductive condition, migratory status, dietary changes, etc)

Thank You

Questions?

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